DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 75-923

Food and Drug Administration
Rockville MD 20857

MAR 24 2004

Endo Pharmaceuticals, Inc.
Attention: Carol Patterson
500 Endo Blvd.
Garden City, NY 11530

Dear Madam:

This letter is being issued on March 24, 2004, to correct an error in the March 23, 2004, approval letter regarding the commencement of 180-day exclusivity.

This is in reference to your abbreviated new drug application (ANDA) dated July 6, 2000, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg, 40 mg and 80 mg.

Reference is also made to your amendments dated January 12, 2001; January 8, 2002; August 20 and 22, October 13 and 16, November 21, 2003; January 7, February 2, February 4, February 12, February 13, February 20, February 27, and March 5, March 9, and March 15, 2004. We also acknowledge receipt of your correspondence dated January 8, 2004, pertaining to the resolution of patent litigation as explained below.

We have completed the review of this abbreviated application, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, final approval of your Oxycodone Hydrochloride Extended-release Tablets, 80 mg, is blocked at this time by another applicant's eligibility for 180-day generic drug exclusivity for the 80 mg strength of this drug product. **Therefore, final approval is granted for your Oxycodone Hydrochloride Extended-release Tablets 10 mg, 20 mg, and 40 mg,** effective March 23, 2004. The 80 mg strength is regarded as tentatively approved, and will be eligible for final approval upon the expiration of the other applicant's 180-day generic drug exclusivity.

The Division of Bioequivalence has determined your Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg, and 40 mg to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Oxycontin® Extended-release Tablets, 10 mg, 20 mg, and 40 mg, of Purdue Pharma LP). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The "interim" dissolution specifications are as follows:

Dissolution testing should be conducted in 900 mL of 0.1 N HCl at 37°C, using (b)(4) . The 10 mg, 20 mg, and 40 mg strengths of the test product should meet the following "interim" specifications:

Time	Percent Dissolved
1 hour	(b)(4)
3 hours	
10 hours	

The "interim" dissolution tests and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement - Changes Being Effected" if there are no revisions to be proposed to the "interim" specifications, or when the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The listed drug product referenced in your application, Oxycontin® Extended-release Tablets, 10 mg, 20 mg, 40 mg, 80 mg, of Purdue Pharma LP., is subject to multiple periods of patent protection. The following United States patents and their expiration dates currently appear in the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations, the "Orange Book":

Patent Number	Expiration Date
4,861,598 (the '598 patent)	August 29, 2006
4,970,075 (the '075 patent)	August 29, 2006
5,266,331 (the '331 patent)	October 26, 2007
5,549,912 (the '912 patent)	October 26, 2007
5,656,295 (the '295 patent)	October 26, 2007
5,508,042 (the '042 patent)	April 16, 2013

Your application contains paragraph IV patent certifications to each of these patents under Section 505 (j)(2)(A)(vii)(IV) of the Act stating that none of the claims of the '598 or '075 patents will be infringed by your commercial manufacture, use, or sale of your Oxycodone Hydrochloride Extended-release Tablets under this ANDA, and that none of the claims of the '331, '912, '042, and '295 patents are valid. Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately unless an action is brought against Endo Pharmaceuticals, Inc. (Endo) for infringement of one or more of the patents which were the subjects of the certifications. This infringement action must be brought against Endo before the expiration of forty-five days from the dates the notices you provided under paragraph (2)(B)(i) were received by the NDA and patent holders. You have notified the Agency that Endo complied with the requirements of Section 505(j)(2)(B) of the Act. As a result, litigation was filed in the United States District Court for the Southern District of New York (the Court) involving your challenge to the '912, '042, and '295 patents for the 40 mg strength (Purdue Pharma L.P., The Purdue Frederick Company, The P.F. Laboratories, Inc., and The Purdue Pharma Company v. Endo Pharmaceuticals Inc., and Endo Pharmaceuticals Holding Inc., Civil Action No. 00-CIV-8029). This suit was amended on two occasions by the defendants following Endo's submission of amendments providing for the 10 mg, 20 mg, and 80 mg strengths (01-CIV-2109). You have notified the Agency that on January 5, 2004, Judge Sidney H. Stein of the District Court dismissed all patent claims against Endo, declared that the '912, '042, and '295 patents are invalid, and enjoined the plaintiffs from enforcing those patents.

With this approval, Endo is eligible for 180-day generic drug exclusivity for Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg and 40 mg as provided for under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments) in Section 505(j)(5)(B)(iv) of the Act. This is because the Agency has concluded that Endo was the first ANDA applicant to submit a substantially complete ANDA for Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg and 40 mg, containing paragraph IV certifications to each patent noted above. This exclusivity will begin to run from the date of first commercial marketing of your Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg, and 40 mg, or from the date of the applicable court decision finding the patent invalid or not infringed, whichever occurs first. [See Section 505(j)(5)(B)(iv)]. Because there was no court decision before December 8, 2003, in which the court found non-infringement or

invalidity with respect to the '912, '042, or '295 patents for ANDAs referencing Purdue Pharma LP's Oxycontin Extended-release Tablets (Oxycodone Hydrochloride Extended-release Tablets) 10 mg, 20 mg, or 40 mg, the court decision that could begin the running of Endo's 180-day exclusivity would be the final decision of a court from which no appeal (other than a petition for a writ of certiorari) has been or can be taken. [See The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Title XI "Access to Affordable Pharmaceuticals", Section 1102(b)(3).

If you have any questions concerning the effective date of approval of an abbreviated new drug application and the Agency's elimination of the requirement that an ANDA applicant successfully defend a patent infringement suit to be eligible for 180-days of marketing exclusivity, please refer to the interim rule published in the November 5, 1998 Federal Register (Volume 63, No. 214, 59710).

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of your Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg, and 40 mg.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns for your Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 20 mg, and 40 mg. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

We are unable to grant final approval to your Oxycodone Hydrochloride Extended-release Tablets, 80 mg, at this time. An ANDA providing for the 80 mg strength of the drug product and containing paragraph IV certifications to the patents listed in the Orange Book was submitted to OGD prior to the submission of your application. Under this circumstance, the applicant of the previously submitted ANDA is eligible for 180-days of generic drug exclusivity for the 80 mg strength. Thus, the Act provides that your Oxycodone Hydrochloride Extended-release Tablets, 80 mg, will be eligible for final approval beginning on the date that is one hundred and eighty days after the date the agency receives notice of the first commercial marketing of the 80 mg strength under the previous application, or the date of a court decision described under Section 505(j)(5)(B)(iv), whichever event occurs earlier. For additional information, we refer you to the agency's guidance document entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments"(June 1988).

Please note that our decision to grant tentative approval to your Oxycodone Hydrochloride Extended-release Tablets, 80 mg, is based upon information currently available to the agency; (i.e., data in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product). This decision is subject to change on the basis of new information that may come to our attention.

In order to reactivate this application to provide for final approval of the 80 mg strength, you must submit a "Supplemental Application - Expedited Review Requested". This supplemental application should be submitted for prior approval approximately 90 days prior to the date you believe that your Oxycodone Hydrochloride Extended-release Tablets, 80 mg, will be eligible for final approval. The supplement should include a detailed explanation of why and when you believe final approval should be granted. It should also include updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This supplemental application should be submitted even if no changes have been made to the application since the date of this tentative approval. Significant changes, as well as an update of the status of the manufacturing and testing facilities' compliance with cGMPs are subject to agency review before final approval of the supplemental application will be granted. We request that you categorize the changes as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt.

In addition to the supplemental application requested above, the agency may request at any time prior to the date of final approval that you submit an additional document containing the requested information. Failure to submit either or, if requested, both documents may result in the rescission of the tentative approval status of your application for Oxycodone Hydrochloride Extended-release Tablets, 80 mg, or may result in a delay in the issuance of the final approval letter.

Please note that under Section 505 of the Act, your Oxycodone Hydrochloride Extended-release Tablets, 80 mg, may not be marketed without final agency approval. The introduction or delivery for introduction into interstate commerce of your Oxycodone Hydrochloride Extended-release Tablets, 80 mg, before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the agency issues the final approval letter, your Oxycodone Hydrochloride Extended-release Tablets, 80 mg, will not be deemed approved for marketing under 21 U.S.C. 355, and will not be listed in the "Orange Book".

Sincerely yours,

(b)(6) [redacted]

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research